

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Axel ULLRICH et al.
Title: FLK-1 IS A RECEPTOR FOR VASCULAR ENDOTHELIAL
GROWTH FACTOR
Prior Appl. No.: 09/766,678
Prior Appl. Filing Date: January 23, 2001
Examiner: Unassigned
Art Unit: Unassigned

INFORMATION DISCLOSURE STATEMENT
UNDER 37 CFR §1.56

Mail Stop PATENT APPLICATION
Commissioner for Patents
PO Box 1450
Alexandria, Virginia 22313-1450

Sir:

Applicants submit herewith on Form PTO/SB/08 a listing of the documents cited by or submitted to the U.S. PTO in parent application Serial No. 09/766,678, filed 01/23/2001; which is a continuation of application Serial No. 08/965,598, filed 11/06/1997, which is a continuation of 08/193,829, filed 02/09/1994, which is a continuation-in-part of application Serial No. 08/038,596, filed 03/26/1993, which is a continuation-in-part of application Serial No. 07/975,750, filed 11/13/1992. As provided in 37 CFR §1.98(d), copies of the documents are not being provided since they were previously submitted to the United States Patent & Trademark Office in the above-identified parent application.

The submission of any document herewith, which is not a statutory bar, is not intended as an admission that such document constitutes prior art against the claims of the present application or that such document is considered material to patentability as defined in 37 CFR §1.56(b). Applicants do not waive any rights to take any action which would be appropriate to antedate or otherwise remove as a competent reference any document which is determined to be a *prima facie* art reference against the claims of the present application.

TIMING OF THE DISCLOSURE

The listed documents are being submitted in compliance with 37 CFR §1.97(b), within three (3) months of the filing date of the application.

Applicants respectfully request that any listed document be considered by the Examiner and be made of record in the present application and that an initialed copy of Form PTO/SB/08 be returned in accordance with MPEP §609.

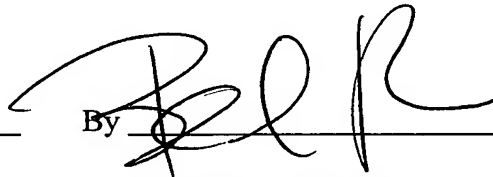
The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 CFR §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741.

Respectfully submitted,

Date

10 March 2004

By



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| | | | | Prior Application Number | 09/766,678 |
| | | | | Prior Appl. Filing Date | 01/23/2001 |
| | | | | First Named Inventor | Axel ULLRICH et al. |
| | | | | Group Art Unit | Unassigned |
| | | | | Examiner Name | Unassigned |
| Sheet | 1 | of | 4 | Attorney Docket Number | 034536-1243 |

| U.S. PATENT DOCUMENTS | | | | | | |
|-----------------------|-----------------------|----------------------|-----------------------------------|---|--|---|
| Examiner Initials* | Cite No. ¹ | U.S. Patent Document | | Name of Patentee or Applicant of Cited Document | Date of Publication of Cited Document MM-DD-YYYY | Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear |
| | | Number | Kind Code ² (if known) | | | |
| | A1 | 5,185,438 | | LEMISHKA | 02-08-1993 | |
| | A2 | 5,712,395 | | APP et al. | 01-27-1998 | |
| | A3 | 5,763,441 | | APP et al. | 06-09-1998 | |
| | A4 | 5,766,860 | | TERMAN et al. | 06-16-1998 | |
| | A5 | 5,792,771 | | APP et al. | 08-11-1998 | |
| | A6 | 5,792,783 | | TANG et al. | 08-11-1998 | |
| | A7 | 5,851,999 | | ULLRICH et al. | 12-22-1998 | |
| | A8 | 5,869,742 | | KÖSTER et al. | 02-09-1999 | |

| FOREIGN PATENT DOCUMENTS | | | | | | | | |
|--------------------------|-----------------------|-------------------------|---------------------|-----------------------------------|--|--|---|----------------|
| Examiner Initials* | Cite No. ¹ | Foreign Patent Document | | | Name of Patentee or Applicant of Cited Documents | Date of Publication of Cited Document MM-DD-YYYY | Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear | T ⁶ |
| | | Office ³ | Number ⁴ | Kind Code ⁵ (if known) | | | | |
| | A9 | WO | 92/03459 | A1 | SLOAN-KETTERING INSTITUTE FOR CANCER RESEARCH | 03-05-1992 | | |
| | A10 | WO | 92/14748 | A1 | AMERICAN CYANAMID COMPANY | 09-03-1992 | | |
| | A11 | WO | 92/17486 | A1 | TRUSTEES OF PRINCETON UNIVERSITY | 10-15-1992 | | |
| | A12 | WO | 94/10292 | A1 | NEUROSPHERES LTD. | 05-11-1994 | | |
| | A13 | WO | 95/21868 | A1 | IMCLONE SYSTEMS INCORPORATED | 08-17-1995 | | |
| | A14 | WO | 96/20403 | A1 | LUDWIG INSTITUTE FOR CANCER RESEARCH | 07-04-1996 | | |

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| OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS | | | | |
|---|-----------------------|--|----------------|--|
| Examiner Initials* | Cite No. ¹ | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published. | T ⁶ | |
| | A15 | BREIER et al., "Expression of Vascular Endothelial Growth Factor During Embryonic Angiogenesis and Endothelial Cell Differentiation," <u>Development</u> 114:521-532, 1992. | | |
| | A16 | CONN et al., "Purification of a Glycoprotein Vascular Endothelial Cell Mitogen From a Rat Glioma-derived Cell Line," <u>Proc. Natl. Acad. Sci. USA</u> 87:1323-1327, 1990. | | |
| | A17 | CONNOLLY et al., "Human Vascular Permeability Factor. Isolation from U937 Cells," <u>The Journal of Biological Chemistry</u> , Vol. 264, No. 33, p.20021, (25 November 1989). | | |
| | A18 | De VRIES et al., "The <i>fms</i> -Like Tyrosine Kinase, a Receptor for Vascular Endothelial Growth Factor," <u>Science</u> 255:989-991, 1992. | | |
| | A19 | FERRARA et al., "Pituitary Follicular Cells Secrete a Novel Heparin-Binding Growth Factor Specific for Vascular Endothelial Cells," <u>Biochem. Biophys. Res. Comm.</u> 161:851-858, 1989. | | |
| | A20 | FERRARA et al., "The Vascular Endothelial Growth Factor Family of Polypeptides," <u>J. Cell Biochem.</u> 47:211-218, 1991. | | |
| | A21 | GOSPODAROWICZ et al., "Isolation and Characterization of a Vascular Endothelial Cell Mitogen Produced by Pituitary-Derived Folliculo Stellate Cells," <u>Proc. Natl. Acad. Sci. USA</u> 86:7311-7315, 1989. | | |
| | A22 | KASHLES et al., "A Dominant Negative Mutation Suppresses the Function of Normal Epidermal Growth Factor Receptors by Heterodimerization," <u>Mol. Cell. Biol.</u> 11:1454-1463, 1991. | | |
| | A23 | KLAGSBURN et al., "Regulators of Angiogenesis" <u>Annu. Rev. Physiol.</u> 53:217-39, 1991. | | |
| | A24 | LEUNG et al., "Vascular Endothelial Growth Factor Is a Secreted Angiogenic Mitogen," <u>Science</u> 246:1306-1309, 1989. | | |
| | A25 | LI et al., "Monoclonal antibodies to recombinant human vascular endothelial growth factor (rHuVEGF)," <u>Journal of Cellular Biochemistry</u> , vol. Suppl., no. 15F, p.251, (1991). | | |
| | A26 | LIVNEH et al., "Reconstitution of human epidermal growth factor receptors and its deletion mutants in cultured hamster cells," <u>J. Biol. Chem.</u> 261(27):12490-12497, 1986. | | |
| | A27 | MAGLIONE et al., "Isolation of Human Placental cDNA Coding For a Protein Related to the Vascular Permeability Factor," <u>Proc. Natl. Acad. Sci. USA</u> 88:9267-9271, 1991. | | |
| | A28 | MATTHEWS et al., "A Receptor Tyrosine Kinase cDNA Isolated From a Population of Enriched Primitive Hematopoietic Cells and Exhibiting Close Genetic Linkage to <i>c-kit</i> ," <u>Proc. Natl. Acad. Sci. USA</u> 88:9026-9030, 1991. | | |

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| (use as many sheets as necessary) | | Attorney Docket Number | 034536-1243 |
| Sheet | 3 | of | 4 |

| OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS | | | |
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| Examiner Initials* | Cite No. ¹ | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published. | T ⁶ |
| | A29 | McCORMICK, "Human gene therapy: The first round," <u>Biotechnology</u> 3(8):689-693, 1985. | |
| | A30 | McMAHON et al., "Protein kinase inhibitors: structural determinants for target specificity," <u>Current Opinions in Drug Discovery and Development</u> 1(2):131-146, 1998. | |
| | A31 | MILLAUER et al., "High affinity VEGF binding and developmental expression suggest Flk-1 as a major regulator of vasculogenesis and angiogenesis," <u>Cell</u> 72:835-846, 1993. | |
| | A32 | MITCHELL et al., "Recombinant Expression and Characterization of the 121 Amino Acid Form of Vascular Endothelial Growth Factor (VEGF)," <u>J. Cell. Biochem., Keystone Symposia on Molecular and Cellular Biology</u> , Supplement 15C, Excerpt G207, 1991. | |
| | A33 | NICOLAS et al., "Retroviral Vectors," <u>Vectors</u> , Chapter 25, pp. 493-494, 1987. | |
| | A34 | ORKIN et al., "Report and Recommendations of the panel to assess the NIH investment in research on gene therapy", December 7, 1995. | |
| | A35 | PLATE et al., "Up-Regulation of Vascular Endothelial Growth Factor and Its Cognate Receptors in a Rat Glioma Model of Tumor Angiogenesis," <u>Cancer Research</u> 53:5822-5827, 1993. | |
| | A36 | PRYWES et al., "Mutations in the cytoplasmic domain of EGF receptor affect EGF binding and receptor internalization," <u>EMBO J.</u> 5(9):2179-2190, 1986. | |
| | A37 | RISAU et al., "Changes in the Vascular Extracellular Matrix During Embryonic Vasculogenesis and Angiogenesis," <u>Development Biology</u> 125:441-450, 1988. | |
| | A38 | SARZANI et al., "A Novel Endothelial Tyrosine Kinase cDNA Homologous To Platelet-Derived Growth Factor Receptor cDNA" <u>Biochem. Biophys. Res. Comm.</u> 186:706-714, 1992. | |
| | A39 | SPIVAK-KROIZMAN et al., "Heterodimerization of c-erbB2 With Different Epidermal Growth Factor Receptor Mutants Elicit Stimulatory or Inhibitory Responses," <u>J. Biol. Chem.</u> 267:8056-8063, 1992. | |
| | A40 | STRAWN et al., "Flk-1 as a Target for Tumor Growth Inhibition," <u>Cancer Research</u> 56:3540-3545, 1996. | |
| | A41 | TARTAGLIA et al., <u>J. Biol. Chem.</u> 267(7), 4304-4307, March 5, 1992. | |
| | A42 | TERMAN et al., "Identification of a New Endothelial Cell Growth Factor Receptor Tyrosine Kinase," <u>Oncogene</u> 6:1677-1683, 1991. | |

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| Examiner Name | Unassigned |
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OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS

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